

In re Application of: Michal DANIELY et al  
 Serial No.: 10/771,440  
 Filed: February 5, 2004  
 Office Action Mailing Date: July 6, 2011

Examiner: Bradley DUFFY  
 Group Art Unit: 1643  
 Attorney Docket: 26003  
 Confirmation No.: 3178

**In the Claims:**

1-71. (Cancelled)

72. (Currently Amended) A method of identifying transitional cell carcinoma cells in a voided urine sample comprising:

(a) staining nucleated cells of the voided urine sample using a stain selected from the group consisting of May-Grünwald-Giemsa, Giemsa, Papanicolau and Hematoxylin-Eosin to thereby obtain stained nucleated cells, and subsequently;

(b) imaging said stained nucleated cells resultant of step (a) so as to obtain images of said stained nucleated cells, and subsequently;

(c) analyzing a nucleus to cytoplasm ratio in transitional epithelial cells by said stain in said images of step (b) and identifying a single cell having a morphological abnormality which comprises a high nucleus to cytoplasm (N/C) ratio as compared to a transitional epithelial cell with a normal morphology, said morphological abnormality indicates that said single cell is suspicious as being a transitional cell carcinoma (TCC) cell, and subsequently;

(d) de-staining said stain of step (a) and subsequently;

~~(de)~~ staining said stained nucleated cells resultant of step (a) using fluorescent *in situ* hybridization (FISH) to thereby obtain nucleated cells stained with FISH, and subsequently;

~~(ef)~~ imaging said nucleated cells stained with FISH resultant of step ~~(de)~~ so as to obtain images of said nucleated cells stained with FISH, and subsequently;

~~(fg)~~ identifying by said FISH in said images of step ~~(ef)~~ a chromosomal abnormality in the same said single cell suspicious as being said transitional cell carcinoma (TCC) cell wherein said chromosomal abnormality indicates that said single cell is a transitional cell carcinoma (TCC) cell;

wherein presence of abnormal nucleus to cytoplasm ratio and said chromosomal abnormality in the same said single cell confirms that said same single cell is a transitional cell carcinoma (TCC) cell,

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thereby identifying the transitional cell carcinoma cells in the urine sample.

73. (Previously presented) A method of diagnosing bladder cancer in a subject, the method comprising:

- (a) obtaining a voided urine sample from the subject;
- (b) identifying transitional cell carcinoma cells according to the method of claim 72,

wherein said presence of said transitional cell carcinoma cell in said voided urine sample is indicative of a positive bladder cancer diagnosis.

74-81. (Cancelled)

82. (Previously presented) The method of claim 72, wherein the transitional cell carcinoma cells are from a bladder cancer or a kidney cancer.

83. (Cancelled)

84. (Previously Presented) The method of claim 72, wherein said imaging is effected using an automated cell imaging device capable of at least dual imaging.

85. (Cancelled)

86. (Cancelled)

87. (Previously presented) The method of claim 72, wherein step (c) further comprising analyzing said transitional epithelial cells for a morphological abnormality selected from the group consisting of an enlarged nucleus, a considerable dark appearance of a cell and an irregular nuclear border as compared to a transitional epithelial cell with a normal morphology.

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88. (Cancelled)

89. (Previously presented) The method of claim 72, wherein said chromosomal abnormality is a polyploidy of a chromosome selected from the group consisting of chromosome 3, chromosome 7 and chromosome 17.

90. (Cancelled)

91. (Previously presented) The method of claim 72, wherein said chromosomal abnormality is a loss of the 9p21 locus.

92. (Cancelled)

93. (Previously presented) The method of claim 72, wherein said nucleated cells of the voided urine sample are cyto-centrifuged at a cell density of 300-500 cells per  $\text{mm}^2$  prior to step (a).